SPECIFICATION AMENDMENTS

(The amendments below are to the 53-page Substitute Specification filed 16 November 2007.)

Rewrite the paragraph running from line 21 of page 18 to line 7 of page 20 as follows:

With the new method and the new device, the desynchronization is carried out qualitatively differently from that of the above described state of the art. Instead of applying signals synchronously to a pathologically effected nerve cell group in a vulnerable phase of its rhythm, the nerve cell group is simply with time coordination stimulated at a number of locations in a manner which causes the desynchronization to arise. For this purpose at the individual stimulation locations either electrical, individual or single pulses can be used or a low frequency stimulation sequence or a high frequency stimulation sequence can be used. It is essential that at least two and preferably more than two stimulation locations be stimulated. If N stimulation locations are stimulated the entire nerve cell population to be desynchronized is subdivided into substantially N equidistant subpopulations (in the phase cycle). [[That]] This means that the phases of the neuronal activity of the subpopulations follow one another in substantially equidistant steps of ~~2π/N, 2π is~~ $2\pi/N$, 2π being the length of a period which has also been defined above as the phase cycle. This utilizes the fact that the pathologically increased interaction between the neurons can contribute to the desynchronization. In this case one utilizes the surprising presence of a self-organization process of the neuronal population which is ~~answerable for the pathological synchronization~~ used to assist in eliminating [[it]] the pathological synchronization.

The same applies where the subdivision of the subpopulations is on an equidistant basis, that is that the subdivision of the total population into subpopulations is effected so that the phases therein will be equidistant and a desynchronization will be accomplished. In contrast thereto, without a pathologically increased interaction, no desynchronization will be effected. The energy of the system itself is thereby utilized to produce a therapeutic effect. An equidistant division into subpopulations is much more easily brought about in a complete desynchronization as with the described methods as the state of the art. The best results are obtained when an equidistant phase shift or a substantially equidistant phase shift of the phase resetting stimuli is applied. From a treatment point of view it is of greater advantage still when the stimulating pulses outputted by the electrodes have the phases of the stimulated subpopulations at least partially shifted relative to one other. The treatment results are better as the phase shift produced approaches an equidistant phase shifting.

SPECIFICATION AMENDMENTS ctd.

Rewrite the paragraph running from line 16 to line 20 of page 21 as follows:

As an individual stimulus or single pulse, a stimulus is intended which can be applied by a single electrode 2. In contrast with a single stimulus reference may be made herein below to a single pulse whereas the single stimulus may be an individual pulse shaped monophasic or biphasic stimulus.

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Rewrite the paragraph running from line 24 of page 34 of line 11 of page 35 as follows:

(b) In case the sensor 3 measures, apart from the illness specific activity additionally also nonillness-specific activity [[,]] from another neuron population, for the estimation of the expression of the pathological feature the feedback signal cannot directly be used. Since the illness-specific activity typically arises in a frequency range different from the frequency range of the [[known]] nonillness-specific activity the estimation of the activity of the illness-specific range is carried out in this case. This can be achieved for example by a frequency analysis. For example the spectral illness in the illness-specific range can be determined. Alternatively after band-pass filtration the amplitude can be determined by measuring the maximum of the band-pass filtered signal or the average value of the magnitude of the signal or after a subsequent Hilbert transformation or by wavelet analysis.

23384AM4.WPD

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        Rewrite the three paragraphs running from line 11 of page
42 to line 25 of page 43 as follows:

        In a time window before the application of the stimulus,
the expression of the pathological feature of the feedback signal
is estimated as in Section 4.4 hereof above. For that purpose, for
example, the amplitude of the oscillating activity in the pathology
specific frequency range is determined by an averaging of the
magnitude of the corresponding band-pass [[path]] filter feedback
signal in a time window prior to the stimulus application. The
strength of the stimulus used is determined by the expression of
the pathological feature as described in Section 4.4. As the
pathological feature is expressed more strongly so the applied
stimulus will be stronger. The control according to the invention
is thus so programmed in this embodiment that it increases the
energy input and the strength of the stimulus signal at the
electrode 2 with the increasing magnitude of the feed back signal.
The relationship between the expression of the pathological feature
and the stimulus strength can in the simplest case be linear,
although it can also have a complex form, for example a nonlinear
form. The stimulus strength can be varied by varying different
stimulation parameters like the number of individual pulses in high
frequency pulse train or low frequency pulse train or the amplitude
of the individual pulses for the duration of the individual pulses.
Preferably the number of individual pulses in the high frequency
pulse train will be varied.
        The number of individual pulses in the high frequency
pulse train which are applied to the kth electrode 2 in the frame
work of the jth total stimulation is indicated as $M_j^{(k)}$ can be
carried out separately for the individual electrodes 2. Preferably

however the matching is carried out for all of the electrodes 2 in the same manner. That means that $M_j^{(k)} = M_j^{(1)}$ for k,1 = 1, 2, 3, ..., N whereby N is the number of electrodes 2. In this case the number of the individual pulses of the high frequency pulse train is given by $M_j = M_j^{(k)}$ for k = 1, 2, 3, ..., N. The device of the invention is thus so programmed that it can vary the stimulation strength in the indicated manner.

As has been described in Section 4.4 above, the expression of the pathological feature, for example, as the amplitude of the oscillating activity in the pathologically specific frequency band, is determined. For this purpose, for example in a time window before the application of the jth stimulus, the magnitude of the illness‑specific frequency range band‑pass [[path]] filter signal is determined. The value determined in this matter is indicated as A_j.

23384AM4.WPD

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Please rewrite the paragraph running from line 11 to line 19 of page 48 as follows:

As has been described in Section 4.4 above, the expression of the pathological feature, for example, as the amplitude of the oscillating activity in the pathologically specific frequency band, is determined. For this purpose, for example in a time window before the application of the jth stimulus, the magnitude of the illness-specific frequency range band-pass [[path]] filter signal is determined. The value determined in this matter is indicated as A_j.

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Rewrite the paragraph running from line 6 of page 45 to line 5 of page 46 as follows:

As described in Section 3.3 hereof, at least one electrode 2 may not be located in the neuron population to be desynchronized. In the case of an electron 2 which does not lie in the neuron population to be desynchronized, the neuron population to be desynchronized is influenced by indirect stimulation as described in Section 3.3 above. Since in the case of an indirect stimulation, the conduction time between the stimulated neuron population on the one hand and the neuron population to be desynchronized on the other can have various values, before carrying out the desynchronization stimulation the respective conduction time is first measured. For this purpose the respective stimulation electrode 2 is stimulated and the stimulation response is measured via the electrodes which has been planted in the neuron population to be desynchronized (sensor 3). This electrode is stimulated indirectly by all of the stimulation electrodes 2 and thus separately n times, where [[by]] n typically is a small whole number up to for example 200. From this the mean conduction time is estimated advantageously in the following manner. The duration between the beginning of the stimulus application over the jth electrode 2 and the first maximum of the stimulation response or the magnitude of the stimulation response, $\tau_j^{(k)}$, is determined for each individual stimulus application. In the magnitude $\tau_j^{(k)}$ the index j stands for the jth electrode 2 while the index k stands for the [[tape]] $\underline{k^{th}}$ applied stimulus. From this, for each stimulation electrode 2 which is to effect an indirect stimulus, separately the mean duration between stimulus beginning and stimulus response is determined in accordance with Formula 4:

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Please rewrite the paragraph running from line 14 to line 18 of page 46 as follows:

If in the direct ~~synchronization~~ <u>stimulation</u> of the neuron population to be desynchronized, a stimulation is to be applied at time t over the jth stimulation electrode, then in the case of the indirect stimulation the jth stimulation electrode 2 will receive the stimulus at the time $t - \tau_j$.

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Rewrite lines 1-27 of page 50 as follows:

Whenever the synchronization of the nerve-cell population exceeds a threshold value, the next total stimulation is outputted over all electrodes. This variant can be used preferentially when the rhythm to be suppressed does not fluctuate too greatly.

2. Repeated stimulation with demand-control duration for the high-frequency pulse train (FIG. 3):

A periodic stimulation is carried out with coordinated stimulus through all electrodes. The strength of the stimulus, [[that]] which is preferably the duration of the high-frequency pulse train, is matched to the strength of the synchronization of the neuron population. The stronger the synchronization the stronger the coordinated stimulus. With this variant, one can select a time delay between the individual stimuli at $\tau/\underline{4}$ [[or]] rather than T/4 where T is the period of the rhythm without stimulation and τ the period forced on the rhythm by the stimulation. In other words, τ is the frequency with which the individual stimuli are applied. The result is a forced oscillation of the system using the single critical stimulation parameter. Instead of an expensive calibration in this context it is dictated by the stimulation period. The demand control stimulation is utilized in any event since the neurons have a pathological tendency to fire or burst periodically or in first (rhythmic production of groups of action potential). Because of this an entrainment easily can arise, that is it is simple in subpopulations to stabilize the periodic rhythm. Because of this form of stimulation requires about 1.5 times less current by comparison to demand control timing.

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Rewrite lines 3-27 of page 52 as follows:

With the device according to the invention with the new
stimulation method, the following illnesses or symptoms can be
alleviated by the desynchronization of suitable framed areas. In
all neurological and psychiatric illnesses in which pathologically
synchronized neuronal activity plays a roll for the expression of
the illness-specific symptom, for example, parkinsonism, essential
tremor, dystony, obsessive disorders, tremor in the case of
multiple ~~scolisis~~ <u>sclerosis</u>, tremor in the case of impact accident
or the like, for example tumorus tissue damage, for example in the
region of the thalamus and/or the [[basil]] <u>basal</u> ganglia,
choreoathetosis and epilepsy, although this listing should not be
considered as limiting.
By the standard measures used to date, the high frequency
continuous stimulation, the following target areas are for example
used:
In the case of parkinsonism, the nucleus subthalamicus or
in the case of tremor dominant parkinsonism, the thalamus, for
example, the <u>ventral intermediate</u> nucleus ~~ventralis intermetius~~
thalami. In the case of essential tremor, the thalamus, for
example, the <u>ventral intermediate</u> nucleus ~~ventralis intermetius~~
thalami. In the case of dystony and choreoathetose the globus
pallidum internum. With epilepsy, the nucleus subthalamicus, the
seraberum, the thalamic nuclear region, for example the <u>ventral</u>
<u>intermediate</u> nucleus ~~ventralis intermetius~~ thalami or the nucleus
caudatus. With obsessive disorder, the capsula interna or the
nucleus accumbens.

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Rewrite lines 9-15 of page 53 as follows:

The invention also encompasses a control which controls
and carries out the required functions with the device according to
the invention as well as the use of the device and the control for
the treatment of parkinsonism, essential tremor, dystony, obsessive
disorder, choreoathetose, tremor with multiple ~~scolisis~~ sclerosis,
tremor in the case of impact injuries or another, for example,
tumorus tissue damage for example in the region of the thalamus
and/or the basal ganglia [[ion]], and epilepsy.